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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,193	05/11/2001	Greta Van Den Berghe	6296.204-US	5893

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 11/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/853,193	VAN DEN BERGHE, GRETA	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-36,40-44 and 62-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-36,40-44 and 62-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The finality of previous Office Action dated April 24, 2006 is withdrawn due to a new ground of rejection.

Status of the Claims

2. Claims 32-36, 40-44 and 62-71 are pending.

Applicant's amendment filed October 24, 2006 is acknowledged, and applicants' response has been fully considered. Claim 86 has been cancelled. Therefore, claims 32-36, 40-44 and 62-71 are examined.

Withdrawn Claim Objections

3. The previous objection to claim 86 is withdrawn in view of applicant's cancellation of the claim in the amendment filed October 24, 2006.

Withdrawn Claim Rejections - 35 USC § 102

4. The previous rejection of claim 86 under 35 U.S.C. 102(b) as anticipated by Scott *et al.* (Stroke 30, 793-799 (1999)), is withdrawn in view of applicant's cancellation of the claim, and applicant's response at page 5 in the amendment filed October 24, 2006.

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 32, 33, 40, 41 and 62-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scott *et al.* (Stroke 30, 793-799 (1999)) in view of Brange *et al.* (U.S. Patent 5,618,913, published on April 8, 1997).

Scott *et al.* teach the use of a 24-hour infusion of saline (control) or a glucose potassium insulin (GKI) infusion (including 16 U of human soluble insulin, 20 mmole of KCl in 500 ml 10% dextrose) at 100ml/h in the treatment of 53 acute stroke patients with mild or moderate hyperglycemia (plasma glucose between 7.0 and 17.0 mmole/L, corresponding to 126 and 307 mg/dL) in an explanatory, randomized, controlled trial to test safety, where no statistically significant differences is detected between the two groups at baseline (Table 1), and the GKI group had lower mean plasma glucose levels at 8 hours (6.4 mmole/L, corresponding to 115 mg/dL), 16 hours (6.5 mmole/L, corresponding to 117 mg/dL) and 24 hours (6.9 mmole/L, corresponding to 124 mg/dL) from the time starting infusion as compared to control, and the mean plasma glucose level is 9.1 mmole/L at zero time of infusion, which corresponds to 164 mg/dL (Table 2; Fig. 1; pages 794-796). The acute stroke patients with no diabetes mellitus in their medical history (Table 1) are human non-diabetic critically ill patients (claims 62- 65). However, Scott *et al.* do not teach the use of an insulin analog in the treatment.

Brange *et al.* disclose some rapid-acting human insulin analogs such as Asp^{B28} human insulin having an improved property such as faster onset of action and reduced tendency to fibrillation as compared to insulin (column 1, lines 56-67; column 2, lines 51-58; claims 33 and 41).

At the time of invention was made, it would have been obvious that one of ordinary skill in the art has been motivated to combine the two references to use an insulin analog as taught by

Brange *et al.* in a method of treating a critically ill patient having a blood glucose level of greater than 130 mg/dl as taught by Scott *et al.* (claims 32, 40) because the use of an insulin analog would provide an improved property such as rapid-acting and reduced tendency to fibrillation as compared to insulin in the treatment (column 1, lines 56-67; column 2, lines 51-58 of Brange *et al.*). Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

6. Claims 32, 34, 40, 42 and 62-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scott *et al.* (Stroke 30, 793-799 (1999)) in view of Anderson, Jr. *et al.* (U.S. Patent 5,547,929, published on August 20, 1996).

Scott *et al.* teach the use of a 24-hour infusion of saline (control) or a glucose potassium insulin (GKI) infusion (including 16 U of human soluble insulin, 20 mmole of KCl in 500 ml 10% dextrose) at 100ml/h in the treatment of 53 acute stroke patients with mild or moderate hyperglycemia (plasma glucose between 7.0 and 17.0 mmole/L, corresponding to 126 and 307 mg/dL) in an explanatory, randomized, controlled trial to test safety, where no statistically significant differences is detected between the two groups at baseline (Table 1), and the GKI group had lower mean plasma glucose levels at 8 hours (6.4 mmole/L, corresponding to 115 mg/dL), 16 hours (6.5 mmole/L, corresponding to 117 mg/dL) and 24 hours (6.9 mmole/L, corresponding to 124 mg/dL) from the time starting infusion as compared to control, and the mean plasma glucose level is 9.1 mmole/L at zero time of infusion, which corresponds to 164 mg/dL (Table 2; Fig. 1; pages 794-796). The acute stroke patients with no diabetes mellitus in their medical history (Table 1) are human non-diabetic critically ill patients (claims 62- 65). However, Scott *et al.* do not teach the use of an insulin analog in the treatment.

Anderson, Jr. *et al.* disclose monomeric insulin analogs such as Lys^{B28}, Pro^{B29} human insulin having a property of ultra rapid time action profile as compared to insulin (column 1, lines 63-67; column 3, lines 2-18; claims 34 and 42).

At the time of invention was made, it would have been obvious that one of ordinary skill in the art has been motivated to combine the two references to use an insulin analog as taught by Anderson, Jr. *et al.* in a method of treating a critically ill patient having a blood glucose level of greater than 130 mg/dl as taught by Scott *et al.* (claims 32, 40) because the use of an insulin analog would provide an improved property such as rapid-acting profile as compared to insulin in the treatment (column 1, lines 63-67; column 3, lines 2-18 of Anderson, Jr. *et al.*). Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

7. Claims 35, 36, 43, 44 and 68-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scott *et al.* (Stroke 30, 793-799 (1999)) in view of Havelund *et al.* (U.S. Patent 5,750,497, published on May 12, 1998).

Scott *et al.* teach the use of a 24-hour infusion of saline (control) or a glucose potassium insulin (GKI) infusion (including 16 U of human soluble insulin, 20 mmole of KCl in 500 ml 10% dextrose) at 100ml/h in the treatment of 53 acute stroke patients with mild or moderate hyperglycemia (plasma glucose between 7.0 and 17.0 mmole/L, corresponding to 126 and 307 mg/dL) in an explanatory, randomized, controlled trial to test safety, where no statistically significant differences is detected between the two groups at baseline (Table 1), and the GKI group had lower mean plasma glucose levels at 8 hours (6.4 mmole/L, corresponding to 115 mg/dL), 16 hours (6.5 mmole/L, corresponding to 117 mg/dL) and 24 hours (6.9 mmole/L,

corresponding to 124 mg/dL) from the time starting infusion as compared to control, and the mean plasma glucose level is 9.1 mmole/L at zero time of infusion, which corresponds to 164 mg/dL (Table 2; Fig. 1; pages 794-796). The acute stroke patients with no diabetes mellitus in their medical history (Table 1) are human non-diabetic critically ill patients (claims 68-71). However, Scott *et al.* do not teach the use of an active derivative of an insulin analog in the treatment.

Havelund *et al.* disclose some active derivatives of insulin analogs such as des-Thr^{B30} human insulin γ Lys^{B29} tetradecanoyl having an improved property such as protracted profile of action and soluble at physiological pH as compared to insulin (column 2, line 27-column 3, line 43; claims 36 and 44).

At the time of invention was made, it would have been obvious that one of ordinary skill in the art has been motivated to combine the two references to use an active derivative of an insulin analog as taught by Havelund *et al.* in a method of treating a critically ill patient having a blood glucose level of greater than 130 mg/dl as taught by Scott *et al.* (claims 35, 43) because the use of an active derivative of an insulin analog would provide an improved property such as prolonged action and soluble at physiological pH as compared to insulin in the treatment (column 2, line 27-column 3, line 43 of Havelund *et al.*). Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusions

8. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PRIMARY EXAMINER

CMK
November 2, 2006